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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,311	BLUMENFELD ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42,43 and 45-73* is/are pending in the application.

4a) Of the above claim(s) *57-63* is/are withdrawn from consideration.

5)☒ Claim(s) *42,59 and 64* is/are allowed.

6)☒ Claim(s) *43,45-56,65 and 68-73* is/are rejected.

7)☒ Claim(s) *66 and 67* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) ~~Paper No(s)~~/Mail Date (2 Sheets)
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the amendment filed November 24, 2003. Applicants arguments and amendments have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. In particular, it is noted that the 102 rejection over Zon as it pertained to claim 50 and as it would apply to newly added claims 65 and 68 is withdrawn in view of Applicants statement that "the as-filed disclosure (which explicitly excluded a polypeptide that has the same amino acid sequence as the murine TBC-1 polypeptide) would have conveyed to one skilled in the art that both the murine TBC-1 polypeptide and the murine TBC-1 polynucleotide of Zon et al were outside the scope of the present invention given the relationship of these two molecules (see for example SEQ ID NO: 1 of Zon et al. providing both the polynucleotide and polypeptide sequences of murine TBC-1)" [see Applicant's comments at page 14 of the response and page 30 of the instant specification.

This action is made final.

Priority

2. Applicant's claim to domestic priority under 35 U.S.C. 119(e) is acknowledged.

Election/Restrictions

3. Applicant's election without traverse of Group I, claims 42-56 and 59 and specifically biallelic marker 9494 of SEQ ID NO: 1 in the response filed April 24, 2003 is acknowledged. The subject matter of the additional biallelic markers and markers in linkage disequilibrium with said markers has been withdrawn from consideration.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

. Claims 43, 45-56 and 59 and newly added claims 65, 68-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acids consisting of SEQ ID NO: 1 or 2, isolated nucleic acids comprising SEQ ID NO: 3 or 4, and isolated nucleic acids consisting of at least 12 contiguous nucleotides of any one of SEQ ID NO: 1-4, does not reasonably provide enablement for nucleic acids comprising SEQ ID NO: 1 or 2, nucleic acids comprising or consisting essentially of 12 contiguous nucleotides of SEQ ID NO: 1-4 or nucleic acids having a "G" at nucleotide position 9494 of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The claims are drawn to polynucleotides consisting of a contiguous span of at least 12 nucleotides of SEQ ID NO: 1 and 2, wherein the span includes the TBC-1

biallelic marker at position 9494 of SEQ ID NO: 1 or a marker in linkage disequilibrium with said biallelic marker; polynucleotides comprising a contiguous span of 8 to 50 nucleotides of SEQ ID NO: 1 or 2 wherein the 3' end of the contiguous span is located 3' upstream within 20 nucleotides of a TBC-1 biallelic marker; and polynucleotides comprising a nucleotide sequence encoding at least 6 amino acids of SEQ ID NO: 5.

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement".

In the instant case, the specification teaches a human genomic DNA sequence which has been set forth in the specification in 2 fragments: the first fragment is set forth in SEQ ID NO: 1 and consists of a 5' untranslated regulatory region, exon 1, exon 1bis, and exon 2; and the second fragment is set forth in SEQ ID NO: 2 and consists of exons A, B, C, D, E, F, G, H, I, J, K, and L and 3' regulatory sequences. The specification also teaches that 2 alternate splice forms of the human nucleic acid

sequence. The first splice form is represented by the cDNA of SEQ ID NO: 3, which consists of a 5' untranslated sequence, exons 1, 2, A, B, C, D, E, F, G, H, I, J, K, and L and a 3' regulatory sequence starting at position 3726. The second splice form is represented by the cDNA of SEQ ID NO: 4, which consists of a 5' untranslated sequence from nucleotides 1 to 175, exons 1bis, 2, A, B, C, D, E, F, G, H, I, J, K, and L and a 3' regulatory sequence. The specification teaches that the human genomic and cDNA sequences share sequence identity with the mouse TBC-1 gene. The mouse TBC-1 gene is set forth, for example, in U.S. Patent 5,700,927 and has been found to be associated with the differentiation of specific types of hematopoietic cells. The specification (see, for example, page 18) also teaches that the human TBC-1 nucleic acid is present in a region of chromosome 4 that has been linked to the occurrence of prostate cancer. Based on this information, the specification (page 6) states that the human TBC-1 gene "is potentially involved in the regulation of the differentiation of various cell types in mammals. A deregulation or an alteration of TBC-1 expression, or alternatively an alteration in the amino acid sequence of the TBC-1 protein may be involved in the generation of a pathological state related to cell differentiation in a patient, more particularly to abnormal cell proliferation leading to cancer states, such as prostate cancer." With respect to biallelic variants, the specification teaches a polymorphism which occurs in intron 1 at position 9494 of SEQ ID NO: 1. Eighteen additional polymorphisms were identified in introns A, B, D, G, H, I and J of the TCB-1 nucleic acid of SEQ ID NO: 2. The specification does not teach any specific functional properties associated with these particular polymorphisms. However, the specification

(page 18) postulates that alterations in the expression of TBC-1 may lead to an altered biological activity which may directly or indirectly cause cell proliferative disorders and diseases associated with abnormal cell proliferation, such as cancer.

The claims as broadly written include a genus of TBC-1 nucleic acids and fragments thereof which are not adequately taught in the specification and for which the specification has not provided sufficient guidance to enable the skilled artisan to use without undue experimentation. The claims encompass nucleic acids which are defined only in terms of the fact that they comprise a polynucleotide that comprises a contiguous span of at least 6 amino acids of SEQ ID NO: 5 or comprise 8 to 50 nucleotides of SEQ ID NO: 12. These polynucleotides read on full length molecules in which only 8 to 50 nucleotides of SEQ ID NO: 1 or 18 nucleotides encoding SEQ ID NO: 5 have been defined and the structure of the remaining nucleotides and function of the molecule is not characterized. The specification makes clear that the claims are intended to encompass all variants of the TBC-1. The claims include nucleic acids encoding all homologs, splice variants, mutants and polymorphic variants of TBC-1 having similar or distinct functional properties. The disclosure of one splice variant and 19 polymorphic variants is not representative of the broadly claimed genus. The specification does not provide sufficient guidance as to what nucleotides may be added to the 3' or 5' terminus of SEQ ID NO: 1 or 2 or to 8-50 mers of SEQ ID NO: 1-2 which will result in a nucleic acid molecule that one of skill in the art could use without undue experimentation. The disclosure of one splice variant in one organism does not provide sufficient information to lead one to make and use additional splice

variants from humans or other species without undue experimentation. While the specification does identify 19 polymorphisms, the TCB-1 genomic DNA spans 18,363 nucleotides and encompasses 14-15 exons. However, polymorphisms have been identified only in 8 introns. This does not constitute a representative number of the polymorphisms that may exist in each of the introns, exons and 5' and 3' untranslated sequences of the human and non-human TBC-1 genes. Additionally, the specification does not disclose any mutations in the TBC-1 gene and specifically does not disclose any mutations associated with the occurrence of proliferative diseases as is encompassed by the claims in view of the teachings in the specification. The claims as amended now include biallelic markers in linkage disequilibrium with the 9494 marker of SEQ ID NO: 1. However, the specification has not taught any markers in linkage disequilibrium with the 9494 marker. Such markers are not defined in terms of their structure and there is no well known structural relationship between the 9494 marker and markers in linkage disequilibrium. No specific guidance has been provided in the specification as to the identity and position of such markers. Accordingly, the specification has not taught a representative number of biallelic markers in linkage disequilibrium with the 9494 marker. Extensive experimentation would be required to identify markers in linkage disequilibrium to meet the broad scope of the claims because this would require extensive experiments of isolating and sequencing numerous additional genomic clones from a representative number of species and identifying polymorphisms which are present in the TBC-1 genes of these species at a frequency of at least 1% and which are in linkage disequilibrium with the 9494 marker.

Furthermore, the specification does not provide adequate guidance as to how to use the biallelic markers or markers in linkage disequilibrium with the biallelic marker. The specification has postulated that these markers may be associated with deregulating or altering the expression of TBC-1 and may be associated with the occurrence of proliferative disorders. However, the specification has not established that any of these polymorphisms are in fact involved in regulating or alerting the expression of TBC-1 or is associated with the occurrence of a cell proliferative disorder. Extensive experimentation would be required to determine which if any of the disclosed polymorphisms are associated with regulation or expression of TBC-1 and with any particular proliferative cell disorder. In the absence of evidence of an association between the structural and functional properties a nucleic acid, it is highly unpredictable as to how the presence of a polymorphism in a coding or non-coding sequence will alter the expression of a nucleic acid or the activity of an encoded protein.

In view of the lack of guidance provided in the specification and the lack of information provided regarding additional TBC-1 homologs, splice variants, mutants and polymorphic variants, undue experimentation would be required to make and use the invention as it is broadly claimed.

RESPONSE TO ARGUMENTS:

In the response filed November 24, 2003, Applicants traverse this rejection by stating that the specification teaches a variety of sequences that can flank the fragments of SEQ ID NO: 1 or 2, including vectors, promoters or enhancers. Applicants

thereby conclude that the specification provides an adequate written description of a variety of elements that can flank the claimed polynucleotides.

Applicants arguments have been fully considered but are not persuasive. Firstly, it is noted that the claims are not limited to polynucleotides in which the sequences flanking the fragments of SEQ ID NO: 1 or 2 are limited to molecules that are vectors, promoters or enhancers. Rather, the claims are inclusive of full length nucleic acid molecules in which only 18 nucleotides are defined in terms of the fact that they encode for a fragment of 6 amino acids of SEQ ID NO: 5 or in terms of the fact that they include a biallelic marker that is encompassed within an 8 to 50 nucleotide fragment of SEQ ID NO: 1 or 2. The identity of the nucleotides flanking the fragments of SEQ ID NO: 1 or 2 or the fragment encoding a portion of SEQ ID NO: 5 are not defined in terms of their structure or function (i.e., a vector, heterologous promoter or heterologous enhancer). The complete polynucleotide sequences claimed are also not defined in terms of their function. Thereby, the claims are inclusive of homologs, splice variants, mutant and polymorphic variants of the human TCB-1 gene. It is also noted that the recitation in claims 65 and 68 of "human polynucleotide" does not further limit the source or structure of the polynucleotide. It is unclear as to what specific structural or functional features would be required to make a polynucleotide a human polynucleotide. What additional nucleotides added to the 18 nucleotides encoding 6 amino acids of SEQ ID NO: 5 would allow one to confirm that a polynucleotide is a "human polynucleotide" versus a "rat polynucleotide" or "rabbit polynucleotide." It is unclear as to whether this limitation is intended to define the polynucleotide based on the method of making the

polynucleotide. Is such a polynucleotide limit to those molecules synthesized in a human cell? Would a TBC-1 gene removed from a naturally occurring rat cell and cloned into a human cell constitute a human polynucleotide? Again, the specification does not clarify what distinguishing features are required to conclude that a polynucleotide is a human polynucleotide. The claims include a very large genus of polynucleotides that may have any functional activity and in particular may have functional activities distinct from the polynucleotide that encodes SEQ ID NO: 5 (i.e., the polynucleotide that comprises SEQ ID NO: 1 and 2). The specification has not adequately taught one of skill in the art how to make a representative number of polynucleotides within the claimed genus and has not adequately taught one of skill in the art how to use such polynucleotides. Furthermore, it is noted that the response did not specifically address the rejection as it applies to polynucleotides which contain a G at nucleotide position 9494. As discussed above, the specification has postulated that these markers may be associated with deregulating or altering the expression of TBC-1 and may be associated with the occurrence of proliferative disorders. However, the specification has not established that any of these polymorphisms are in fact involved in regulating or alerting the expression of TBC-1 or is associated with the occurrence of a cell proliferative disorder. Undue experimentation would be required for the skilled artisan to use the polynucleotides containing a G at position 9494 of SEQ ID NO: 1 because the specification has not established that this polymorphism is associated with regulation or expression of TBC-1 and with any particular proliferative cell disorder. Additionally, in view of the amendment to the claims, the specification has also not

enabled markers in linkage disequilibrium with the 9494 marker. The specification has not taught any such markers and has not provided any specific guidance for obtaining such markers. It is unpredictable as to what would be the identity of such a marker. Further, it is unpredictable as to how to use such a marker since the specification has not taught that such a marker is correlated with regulation or expression of TBC-1 or with any proliferative cell disorder. The ability to randomly search for markers which are in linkage disequilibrium with the 9494 marker is not equivalent to teaching one how to make specific polynucleotides containing specific biallelic markers.

5. Claims 43, and 45-56 and newly added claims 65 and 68-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polynucleotides consisting of a contiguous span of at least 12 nucleotides of SEQ ID NO: 1 and 2, wherein the span includes the TBC-1 biallelic marker at position 9494 of SEQ ID NO: 1 or a marker in linkage disequilibrium with said biallelic marker; polynucleotides comprising a contiguous span of 8 to 50 nucleotides of SEQ ID NO: 1 or 2 wherein the 3' end of the contiguous span is located 3' upstream within 20 nucleotides of a TBC-1 biallelic marker; and polynucleotides comprising a nucleotide sequence encoding at least 6 amino acids of SEQ ID NO: 5.

The specification teaches a human genomic DNA sequence comprising a first fragment which is set forth in SEQ ID NO: 1 and consists of a 5' untranslated regulatory region, exon 1, exon 1bis, and exon 2; and a second fragment which is set forth in SEQ ID NO: 2 and consists of exons A, B, C, D, E, F, G, H, I, J, K, and L and 3' regulatory sequences. Two alternate splice forms of this nucleic acid sequence are also taught. The first splice form is represented by the cDNA of SEQ ID NO: 3, which consists of a 5' untranslated sequence, exons 1, 2, A, B, C, D, E, F, G, H, I, J, K, and L and a 3' regulatory sequence starting at position 3726. The second splice form is represented by the cDNA of SEQ ID NO: 4, which consists of a 5' untranslated sequence from nucleotides 1 to 175, exons 1bis, 2, A, B, C, D, E, F, G, H, I, J, K, and L and a 3' regulatory sequence. The specification teaches that the human genomic and cDNA sequences share sequence identity with the mouse TBC-1 gene. The mouse TBC-1 gene is set forth, for example, in U.S. Patent 5,700,927 and has been found to be associated with the differentiation of specific types of hematopoietic cells. The specification (see, for example, page 18) also teaches that the human TBC-1 nucleic acid is present in a region of chromosome 4 that has been linked to the occurrence of prostate cancer. Based on this information, the specification (page 6) states that the human TBC-1 gene "is potentially involved in the regulation of the differentiation of various cell types in mammals. A deregulation or an alteration of TBC-1 expression, or alternatively an alteration in the amino acid sequence of the TBC-1 protein may be involved in the generation of a pathological state related to cell differentiation in a patient, more particularly to abnormal cell proliferation leading to cancer states, such as

prostate cancer." With respect to biallelic variants, the specification teaches a polymorphism which occurs in intron 1 at position 9494 of SEQ ID NO: 1. Eighteen additional polymorphisms were identified in introns A, B, D, G, H, I and J of the TCB-1 nucleic acid of SEQ ID NO: 2. The specification does not teach any specific functional properties associated with these particular polymorphisms and does not teach any polymorphisms in linkage disequilibrium with the biallelic markers. The specification (page 18) postulates that alterations in the expression of TBC-1 may lead to an altered biological activity which may directly or indirectly cause cell proliferative disorders and diseases associated with abnormal cell proliferation, such as cancer.

The claims as broadly written do not meet the written description requirements of 35 U.S.C. 112, first paragraph, because the specification does not disclose and fully characterize the genus of any homolog, splice variant, biallelic variant or mutant form of TBC-1. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of

a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the prior art teaches one murine TBC-1 cDNA and the specification teaches 2 splice forms of the human TBC-1 genomic and cDNA as well as 19 polymorphisms in the introns of the TBC-1 gene. This does not constitute a representative number of members encompassed by the genus of any nucleic acid comprising 8 to 50 nucleotides of SEQ ID NO: 1 or 2 or comprising a fragment that encodes 6 amino acids of SEQ ID NO: 5 or consisting at least 12 nucleotides of SEQ ID NO: 1 or 2 and including a biallelic marker in linkage disequilibrium with the biallelic marker 9494 , wherein the flanking nucleotides and the functional activity of the nucleic acid are not defined and/or the identity and location of the marker in linkage disequilibrium is not defined. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g., in terms of functional activity, or in terms of being in linkage disequilibrium with other well characterized polymorphisms, etc). In the instant case, no such identifying characteristics have been provided for any additional flanking sequences. Defining a polymorphism in terms of the fact that it is in linkage

disequilibrium with the marker 9494 does not further define the identity and location of the polymorphism. The broadest reasonable interpretation of the claims indicates that the claims are inclusive of a genus of biallelic markers present at any position in any TBC-1 gene, including the 3' and 5' untranslated regions, exon and intron regions of the TBC-1 genes, splice variants and mutant forms of TBC-1. While one could contemplate a nucleotide substitution at each and every position in the TBC-1 gene, such substitutions are not considered to be equivalent to specific polymorphisms associated with TBC-1 regulation or expression or associated with cell proliferative disorders. Rather, polymorphisms and mutations associated with TBC-1 regulation and expression and with the occurrence of specific diseases represent a distinct group of nucleotide variations which are expected to occur at only specific locations within the gene and consist of specific nucleotide alterations. Accordingly, knowledge of the sequence of the wild-type TBC-1 gene does not allow the skilled artisan to envision all of the contemplated polymorphisms, mutations, splice variants and homologs encompassed by the claimed genus in which the sequences flanking small portions of SEQ ID NO: 1 or 2 are not defined and in which the polymorphism in linkage disequilibrium with the 9494 marker is not defined. Therefore, Applicants have not provided sufficient evidence that they were in possession, at the time of filing, of the invention as it is broadly claimed and thus the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1

"Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

RESPONSE TO ARGUMENTS:

In the response filed November 24, 2003, Applicants traverse this rejection by stating that the claims as amended have rendered the above rejection moot.

However, the amendment to claim 43 and the claims that depend therefrom has not rendered the rejection moot. The amendment has modified the claims to include polynucleotides comprising a biallelic marker that is in linkage disequilibrium with the 9494 marker. However, the specification has not adequately described a representative number of markers in linkage disequilibrium with the 9494 marker in terms of their structure. There are no teachings in the specification as to the location and identity of such markers. Further, the teachings in the specification regarding the identity of the 9494 marker does not provide adequate written support for a marker in linkage disequilibrium with the 9494 marker. The specification does not teach a clear structural relationship between the markers such that knowledge of the 9494 marker would allow one to envision other specific markers in linkage disequilibrium with the 9494 marker. Furthermore, the amendment does not overcome the issues raised above concerning claims 48-56 and newly added claims 65 and 68-73. These claims are not adequately defined in terms of their structure since these claims define only a small fragment of the overall polynucleotide (e.g., an 8 to 50 nucleotide fragment of SEQ ID NO: 1 or 2 containing the 9494 marker or a marker in linkage disequilibrium with the 9494 marker; or a fragment encoding 6 amino acids of SEQ ID NO: 5). Further, these claims do not

define the functional properties of the polynucleotide. As discussed above, these claims include full length TBC-1 homologs, splice variants, mutant and polymorphic variants and the teachings in the specification of 2 alternate splice forms of human TBC-1 and 19 polymorphic variants is not representative of the broadly claimed genus of polynucleotides.

6. Claims 66 and 67 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)-272-0782. Papers related to this

application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers
February 4, 2004

CARLA J. MYERS
PRIMARY EXAMINER